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receptor (MC5-R) with a proopiomelanocortin (POMC) compound which binds to and activates said melanocortin receptor in the presence and absence of a putative regulatory compound;

b. detecting whether said putative regulatory compound inhibits said melanocortin receptor activity;

wherein putative regulatory compounds that inhibit said melanocortin receptor activity are identified as compounds that increase body weight by regulating peripheral pathways of energy homeostasis.

Sub B2
19. (Once Amended) A method for identifying compounds that regulate peripheral pathways of energy homeostasis, comprising:

(a) contacting a putative regulatory compound with an isolated adipocyte;

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and,

(b) detecting putative regulatory compounds that bind to a melanocortin receptor on said adipocyte, wherein putative regulatory compounds that bind to melanocortin receptors on said adipocytes are identified as compounds that regulate body weight by regulating peripheral pathways of energy homeostasis.

Please add the following new Claims 22-29.

Sub B3
22. (Added) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors, comprising:

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a. contacting a putative regulatory compound with a cell which expresses a melanocortin receptor that is expressed in the peripheral tissues;

b. detecting whether the putative regulatory compound increases activity of said melanocortin receptor;

c. contacting said putative regulatory compound with a cell which expresses a melanocortin 4-receptor (MC4-R); and,

d. detecting whether the putative regulatory compound increases MC4-R activity;

Sur B3
wherein putative regulatory compounds that induce greater activity by said melanocortin receptor that is expressed in the periphery as compared to said MC4-R are identified as compounds that preferentially bind to and activate peripheral melanocortin receptors.

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cont.
23. (Added) The method of Claim 22, wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of melanocortin receptor ligand binding activity, measurement of G protein activation, and measurement of melanocortin receptor translocation within a cell.

24. (Added) The method of Claim 22, wherein said cell of step (a) is an adipocyte, and wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of G protein activation, measurement of melanocortin receptor ligand binding activity, measurement of melanocortin receptor translocation within a cell, measurement of lipolysis by said cell and measurement of free fatty acid uptake by said cell.

25. (Added) The method of Claim 22, wherein said step (d) of detecting is selected from the group consisting of measurement of MC4-R transcription, measurement of MC4-R translation, measurement of phosphorylation of MC4-R, measurement of MC4-R ligand binding activity, and measurement of MC4-R translocation within a cell.

Sur B4
26. (Added) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors, comprising:

- a. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a melanocortin receptor that is expressed in the periphery;
- b. detecting expression of the reporter gene product;

c. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a melanocortin 4-receptor (MC4-R); and,

d. detecting expression of the reporter gene product;

wherein putative regulatory compounds that increase expression of the reporter gene product of (b) as compared to the reporter gene product of (d) are identified as compounds that preferentially bind to and activate peripheral melanocortin receptors.

27. (Added) A method for identifying compounds for increasing body weight by inhibition of peripheral melanocortin receptors, comprising:

a. contacting a putative regulatory compound with a cell or cell lysate containing transcripts of a melanocortin receptor that is expressed in the periphery; and,

b. detecting translational inhibition of the melanocortin receptor transcript;

wherein putative regulatory compounds that inhibit said melanocortin receptor transcript are identified as compounds that inhibit peripheral melanocortin receptor expression.

28. (Added) A method for identifying compounds that regulate peripheral melanocortin receptors, comprising:

(a) contacting a putative regulatory compound with an isolated adipocyte; and,

(b) detecting putative regulatory compounds that bind to a melanocortin receptor on said adipocyte, wherein putative regulatory compounds that bind to melanocortin receptors on said adipocytes are identified as compounds that regulate peripheral melanocortin receptors.

29. (Added) The method of Claim 28, wherein said step of detecting further comprises detecting putative regulatory compounds which produce a result selected from the group consisting of stimulation of lipolysis in said adipocytes and inhibition of the uptake of fatty acids by said adipocytes, wherein putative regulatory compounds that bind to

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cont.

melanocortin receptors on said adipocytes and that produce said result are identified as compounds that regulate peripheral melanocortin receptors.

add p5